Technical Note

Documentation of a New Intracavitary Applicator for Transrectal Hyperthermia Designed for Prostate Cancer Cases: A Phantom Study

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Abstract

Concerning clinical trials, intracavitary hyperthermia has already shown antitumor activity and has a potential role in the treatment of prostate cancer. The aim of this study was to document a new intracavitary applicator operating at 433 MHz, designed for transrectal hyperthermia, as well as to assess the specific absorption rate (SAR) distributions in terms of temperature measurements in a soft-tissue phantom. The microwave applicator consists of a dipole-type λ/2, a reflector, and the cooling system. The applicator was placed into a soft-tissue gel-phantom box that was mimicking the dielectric properties of the normal tissue. A calibrated thermometer was implanted inside the phantom at specific locations, to calculate temperature distributions. The maximum value of the SAR was 108 W/kg on the surface's central area at the footprint of the antenna, while the penetration depth was at around 3 cm. Our experimental measurements confirmed the role of the reflector concerning the directivity in a certain area and non icotropic, by means of protecting normal tissues around the prostate. The SAR experimental measurements showed that our applicator might be used effectively as a treatment device for prostate cancer, demonstrating a clear advantage over other similar transrectal devices.

Keywords: Hyperthermia, microwave, phantom, specific absorption rate, transrectal

Received on: 12-06-2017 **Review completed on:** 11-02-2018 **Accepted on:** 13-02-2018

Introduction

The high prevalence of prostate cancer in the general population has led to exceptional changes in treatment during the past century, while the standard treatment for early prostate cancer is surgery or radiation therapy combined with hormone therapy.[1,2] In cases of recurrence of disease after failure of radiation therapy, optimal treatment remains unclear.[3] Several studies[3,4] have shown that hyperthermia combined with radiation appears as a promising therapy of locally advanced prostate cancer by enhancing the efficacy of treatment and survival rate of patients.[4]

Intracavitary hyperthermia, as a rapidly developing treatment has led to the improvement of standard systems and the creating of more flexible and adaptive applicators.[5] The aim of this study is to document a new intracavitary microwave hyperthermia applicator specially designed for heating prostate through the rectal operating at 433 MHz, as well as to evaluate the specific absorption rate (SAR) distributions in terms of temperature measurement in a soft-tissue phantom.

Subjects and Methods

Applicator design

The proposed hyperthermia applicator [Figure 1] is composed of a dipole-type λ/2, a conductive semicylindrical reflector and the cooling liquid that flows around the applicator to prevent

Access this article online	
Quick Response Code:	**Website:** www.jmp.org.in
	DOI: 10.4103/jmp.JMP_67_17

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How to cite this article: Kouloulias V, Nikolakopoulou A, Karanasiou I, Antypas C, Armpilia C, Uzunoglou N. Documentation of a new intracavitary applicator for transrectal hyperthermia designed for prostate cancer cases: A phantom study. J Med Phys 2018;43:141-5.

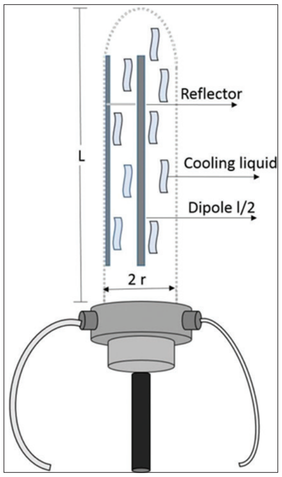

Figure 1: The construction of the intracavitary hyperthermia applicator

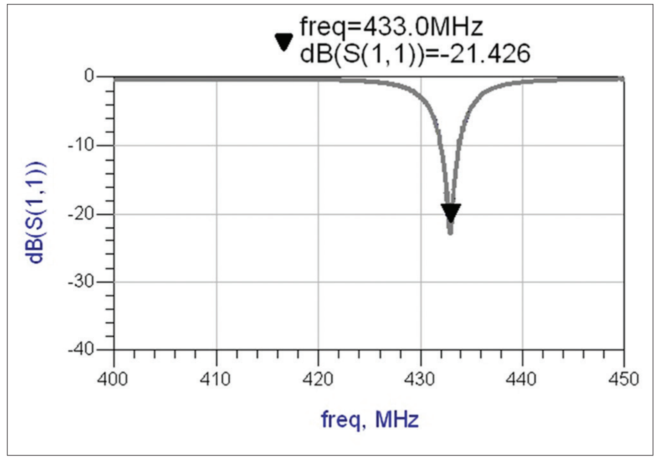

Figure 2: Measurement of S11 performance

overheating of conducting rectal mucosa. It was designed to operate at 433 MHz with a total length of 15 cm and a diameter of 3.5 cm. The main function of the reflector is to give directional characteristics to the applicator. The outer structure of the applicator is a Teflon-like solid biocompatible plastic. Mixtures of ethylene glycol and water are used as a coolant liquid. Ethylene glycol has desirable thermal properties including a high boiling point, low freezing point, stability over a wide range of temperatures, and high-specific heat and thermal conductivity.

The applicator was calibrated in laboratory to ensure the matching with transmission lines of power at 50 ohm. Measurements of antenna impedance are described by determining S11. S-parameters describe the relationship between input and output ports in an electrical system. One of the most commonly used parameters regarding antenna performance is S11. It represents the amount of power reflected from the antenna and thus, how well the antenna is matched to the rest of the system. S11 is a measure of the performance of the antenna as an efficient radiator. Particularly, antenna was connected through a short 50 ohm cable and the short stubs to the vector network analyzer as described by Kouloulias *et al*.[6] An adjustment of the antenna input impedance was performed to achieve the suitable antenna matching, over a range of different tissue impedance loads at the intended driving frequency of 433 MHz. The measurement of S11 performance is shown in Figure 2.

Soft-tissue phantom

The applicator was immersed into a soft-tissue phantom box [Figure 3a] that is introduced as a new tissue-mimicking phantom for the purpose of two-dimensional temperature distribution during microwave ablation. The phantom is transparent and the physical properties of the phantom, such as density, electrical conductivity, and specific heat capacity, are very favorable, similar to those of biological soft tissue at microwave frequencies. The phantom size is big enough to provide zero heating power at the outer boundary of phantom load as well as to eliminate any foreground reflections off the side walls of phantom container. Particularly, the length, the width, and the wall thickness of the box were measured as 30 cm, 16 cm, and 5 mm, respectively. The composition of the soft-tissue phantom is water (1.8340 kg), sucrose (1.5785 kg), sodium chloride (0.0490 kg), and gelatine (0.0385 kg). Soft-tissue phantom was preserved in a semi-fluid state through freezing procedure at 5°C, while it was tested for its dielectric properties by coaxial lines, as described by Kouloulias *et al*.[7] In a typical operation, the applicator is inserted into the rectum with its active surface facing the prostate. The absolute requirements in the design of the applicator are related to the anatomical structures of the prostate and the surrounding tissues as shown in Figure 3b. In spite of the high temperatures, the rectal tolerance is not affected by these treatment conditions, due to the fact that the surface of this applicator is cooling the rectal mucosa through circulating water in the closed circuit of the applicator, as shown in Figure 1.

Specific absorption rate measurements

Experimentally, SAR can be calculated from the rate of temperature rise in tissues exposed to high-power electromagnetic (EM) fields, according to this formula: SAR = 4186 c $\Delta T/\Delta t$ (w/kg), where c is the specific heat in kcal/kg °C, ΔT the temperature rise in °C, and t the exposure in time in seconds.[8] In this study, the SAR distributions were calculated from the temperature measurements where the specific heat of phantom was 0.86 kcal/kg °C and the heating period was 60 s.

The measurements were made using a hyperthermic microwave system 433 MHz, consisting of three main parts: a power unit, a microwave signal generator, and two amplifiers.[9,10] All experiments were performed for output MW maximum power equal to 100 W. The distribution of the temperature along the applicator was measured with an invasive thermometer implanted in the selected points of measurements (separated by 1 cm) in the soft-tissue phantom box [Figure 4]. SAR measurements separated by 1 cm were also made at same selected points at three different areas at 1, 2, and 3 cm depth,

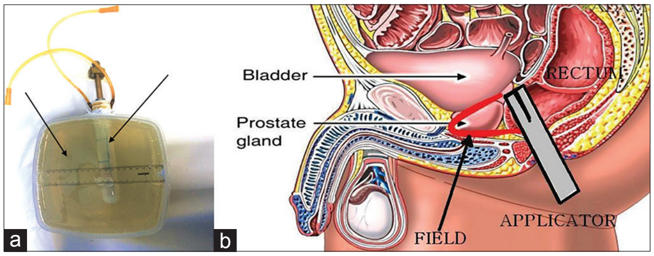

Figure 3: (a) Phantom box with the inserted microwave applicator. (b) Anatomical site of prostate and conjunction structures with the applicator sited intrarectally simulating an intracavitary hyperthermia treatment (Red line represents the expected heating field.)

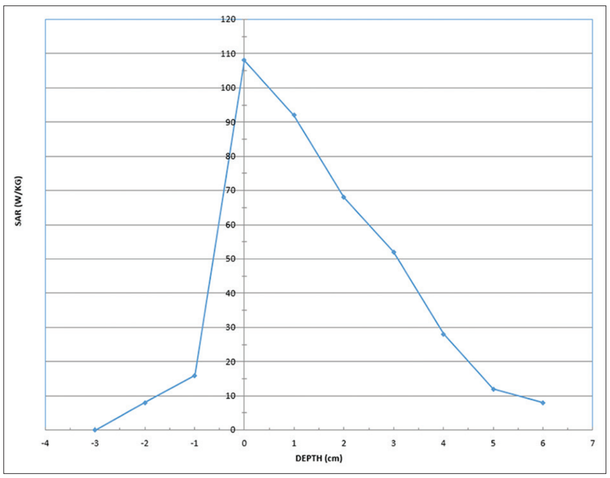

Figure 5: Specific absorption rate penetration curve at the center of the applicator

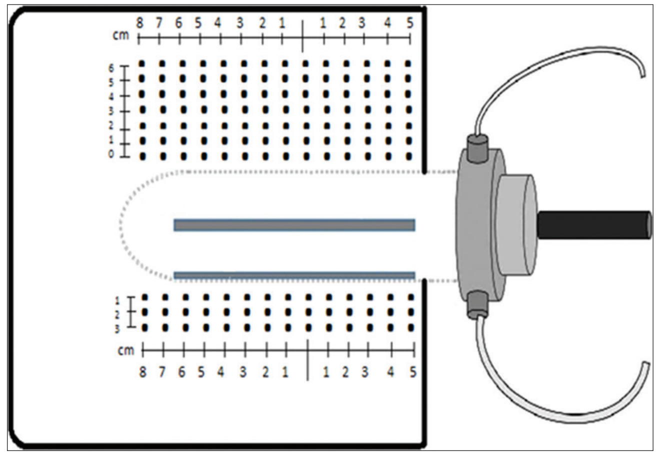

Figure 4: The points of temperature measurements at the central plane of the applicator

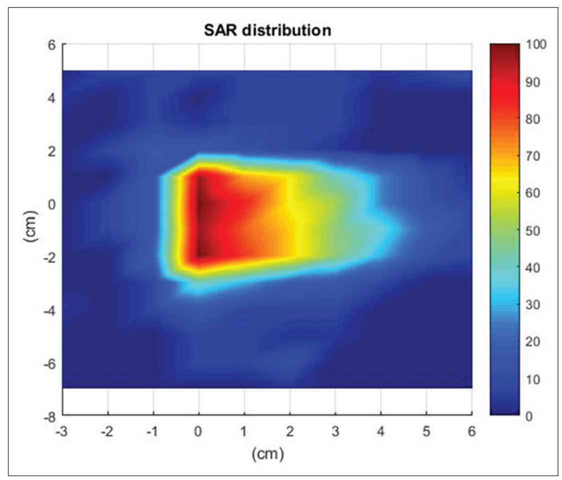

Figure 6: The specific absorption rate distribution along the applicator in the central plane

respectively, inside the phantom, below and along the central region (plane) of the applicator, with respect to all selected points within the corresponding regions. The data were saved in the system database. However, it should be mentioned that our experimental measurements could also be confirmed with an infrared camera.

Results

Figure 5 shows SAR penetration curve at the center of the applicator. It is shown that the level of SAR decreases with increasing depth, while the highest SAR value observed in the center of the applicator surface was calculated to be 108 W/kg. SAR distribution, when SAR values are normalized from 1% to 100%, along the antenna is presented in Figure 6. The degradation of the color from blue to red represents increasing normalized SAR values from 1% to 100%. Figures 5 and 6 show that microwave power is mainly absorbed in the region close to the applicator surface. The depth at which the SAR value is the half of the maximum rate observed in the surface of the antenna in the biological tissue or the phantom is defined as penetration depth. According to our measurements, as shown in Figure 5, penetration depth can be estimated as 3 cm and the width of 50% SAR distribution was assessed as 5 cm along the main axis of the dipole $\lambda/2$. There is a 25% decrease in the maximum SAR value 4 cm away from the tip of the applicator. The majority of SAR values were approximately zero, 3cm away from the tip of the applicator as the results show. As shown in Figures 5 and 6, minimum SAR values have been calculated in the backward direction where the reflector is located. Particularly, normalized SAR rates in the backward direction behind the reflector were approximately zero. Finally, Figures 5 and 6 show the directional effect obtainable with a single conductive material (reflector). In addition, SAR measurements were made at 1, 2, and 3 cm depth, respectively, inside the phantom, below and along the central axis of the applicator to assess the temperature variation within target volume, and confirm the decreasing of energy absorbed in the below regions away from the central plane of the applicator [Figure 7]. As shown in Figure 7, the SAR distribution values decreased through the planes of 1, 2, and 3 cm depth inside the phantom compared to the SAR values taken along the applicator central plane as presented in Figure 6.

Discussion

The effectiveness of hyperthermic therapy is directly related to the temperature achieved during treatment, the length of treatment, cell and tissue characteristics, and finally the capability of the applicators to deliver energy successfully into a tumor.[11,12] Concerning the penetration depth in clinical practice, the range is typically limited to 3–4 cm and depends on the frequency and applicator size.[5,8] In this study, the penetration depth was measured to be 3 cm. Another interesting point delivered from this study is the protection of rectal mucosa surface during hyperthermia procedure. In particular, the treatment includes rectal cooling with cooling water through the applicator surface contacting the rectal wall to reduce the local rectal mucosa heating.

Over the years, a number of researchers have suggested various design applicators used for hyperthermia in prostate cancer. Vrba *et al*.[13] presented the heating pattern obtained from three different microwave antennas: the monopole, the dipole, and the helical coil, developed for prostate cancer. In their study, it was demonstrated that microwave power was emitted isotropically around the three antennas. On the contrary, our results showed that the microwave energy was absorbed only in the area of interest, confirming the role of the reflector to direct the microwave energy towards in a certain area. Biffi Gentili *et al*.[14] presented a dipole-type applicator together with theoretical EM and thermal models capable of evaluating temperature distribution in a polyacrylamide phantom. The temperature distribution and the consideration of specific curves in lower or in higher temperatures of the cooling liquid were investigated. The penetration depth of the EM wave from the applicator was limited compared to the penetration of microwaves in our device by means of sufficient heating of larger tumors seated in greater depth inside the human body. Franconi *et al*. developed radiofrequency (RF) applicators with controlled dielectric matching interfaces for evaluating output RF radiation in intracavitary and in interstitial prostate hyperthermia therapy using phantom tissues. The proposed devices presented customizable length and shape, independence of insertion depth, uncritical air gap, and longitudinal heating uniformity. However, the transfer of RF energy was poor causing limited penetration depths (19–20 mm).[15]

The main problem associated with any hyperthermia technique is the need to control the temperature distribution of absorbed power in the tissue or mimicking phantom during hyperthermia procedure. However, creating durable phantoms

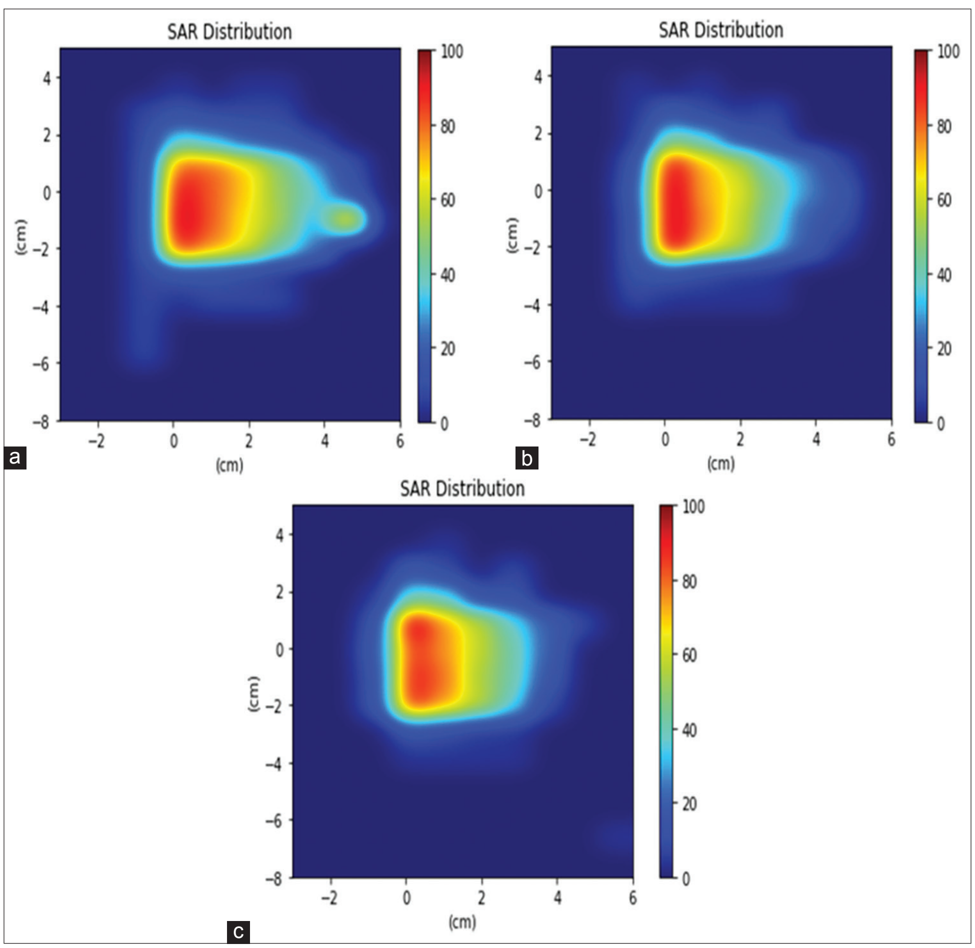

Figure 7: The specific absorption rate distribution inside the soft-tissue phantom, below the central plane of the applicator at: (a) 1 cm depth, (b) 2 cm depth and (c) 3 cm depth.

with high precision level to represent SAR distribution is under investigation.[16] The described phantom is an attractive tissue-mimicking phantom suitable for microwave investigations. The design of the applicator presented in this study has shown good SAR distribution in the area of interest and desired penetration depth into the phantom material. It seems that the current applicator is capable of effectively transferring heat only to one side of the antenna. Consequently, the proposed antenna might be used as a treatment device for prostate cancer, demonstrating a clear advantage over other similar applicators with isotropic SAR distribution.

Concerning the clinical situations to the current work, it must be mentioned that there is a variety of different parameters that must be considered if the proposed hyperthermia device is going to be used combined with either radiotherapy or high-dose rate brachytherapy treatments at the same time. For instance, the brass (located at the base of our applicator) could ineffectively modify the dose distribution across the beam. As a result, evaluation of beam hardening and photon scatter by brass is definitely required. Moreover, the attenuation of the microwave applicator and the thickness and attenuation of the reflector system must be taken into account for radiation dosimetry. However, the biological advantage of combining hyperthermia and radiation therapy simultaneously has led to the development of techniques for simultaneous hyperthermia and external beam radiation therapy.[17] In addition, another parameter to take into account is the potential radiobiological effect of combined hyperthermia with radiation therapy or lower doses of radiotherapy in cases after re-irradiation of patients with prostate cancer using biological modeling. Van Leeuwen *et al*.[18] developed a 3D radiobiological model to evaluate the combination of radiotherapy and hyperthermia, capable to be used for individualized treatment decisions and treatment optimization. However, radiobiological evaluation of combined hyperthermia with radiation therapy, for prostate cancer cases, remains an aspect for further investigation.

Conclusion

Our device enables deep heat penetration promising improved treatment outcome, as well as the ability to increase temperature and easily direct the microwave energy toward prostate while, at the same time, ensuring that healthy tissue is not overheated. However, the clinical application of the proposed antenna can be performed only after simulations using realistic clinical setups through treatment planning based on anatomical structures of human body, to achieve patient-specific treatment. Finally, modeling of hyperthermia tumor effect and the possible effects in neighboring healthy tissues which should be based on detailed treatment planning simulation procedure will be a powerful future tool for optimizing treatment quality and enhancing treatment planning.[19]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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